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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
05/05/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

SIP_Docket@mwe.com

Office Action Summary	Application No.	Applicant(s)	
	10/727,655	SZELENYI ET AL.	
	Examiner	Art Unit	
	Brian-Yong S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02/19/09*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-28* is/are pending in the application.

4a) Of the above claim(s) *16-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-15 and 23-28* is/are rejected.

7)☐ Claim(s) _ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/15/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Acknowledgement is made of applicant's filing of amendment/remarks on 02/19/2009. By the amendment, claims 12-15 have been amended and claim 28 has been newly added. Claims 12-15 and 24-28 are currently pending for prosecution on the merits of the case.

2. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 12, 14 and 23-28 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses that the mechanism of inhibiting Na+ channels could contribute to reducing muscle tone and produce the pain-alleviating effect. The specification discloses namely tolperisone, eperisone, silperisone, riluzole, propafenone, lidocaine, flecainide and metixen as a suitable example of a sodium channel-inhibiting substance, which meet the written description and enablement provisions of 35 USC 112, first paragraph. However, the

claims 12, 14 and 23-27 are directed to encompass "a sodium channel-inhibiting substance" such as antagonists or partial antagonists of sodium channel including sodium/hydrogen exchangers, sodium-glucose transporters, sodium/myoinositol cotransporter, Na+/I- symporter, sodium/potassium/calcium exchanger, Na+/K+/CI- cotrasporter and etc... which only correspond in some undefined way to specifically instantly disclosed chemicals. None of these meet the written description provision of 35 USC 112, first paragraph, due to lacking chemical structural information for what they are and chemical structures are highly variant and encompasses a myriad of possibilities. To the extent that no structure function data is disclosed in connection with theses functionally described compounds to correlate, or there is not disclosed correlation established between these functional drugs and the contemplated desired therapeutic effect to be achieved in practicing the instant invention, the specification provides insufficient written description to support the genus encompassed by the claims.

Vas-Cath Inc. Mahurkar, 19 USPQ2d 1111, makes clear the "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of tolperisone, eperisone, silperisone, riluzole, propafenone, lidocaine, flecainide and metixen, the skilled artisan cannot envision the detailed chemical structure of the encompassed inhibitors or antagonists or mixed agonist/antagonists of sodium/hydrogen exchangers, sodium-glucose transporters, sodium/myoinositol cotransporter,

Na+/I- symporter, sodium/potassium/calcium exchanger, Na+/K+/CI- cotrasporter etc., regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

…To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966(1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)* ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.*

It is noted to applicant that this rejection could be obviated by amending "a sodium channel-inhibiting substance" to "a voltage-gated sodium channel inhibitor".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 12-13 and 23-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rundfeldt et al. (US 6117900) in view of Cai et al. (US 6281211), and further in view of the applicant's admitted prior art of the record (page 1, line 25 through page 4, line 3).

Rundfeldt teaches the use of retigabine for the treatment of neuropathic pain in an animal, wherein said compound is administered in various dosage forms including oral or parenteral forms (abstract; column 8, lines 26-37; claims).

Cai teaches the use of Na+ channel blocker such as riluzole, lidocaine, propafenone and semicarbazone derivatives for the treatment neuropathic pain in mammals including humans (see particularly "Related Background Art" in column 1, lines 18-56 and "Summary of Actions"; abstract).

Applicant's admitted prior art of records teaches the use of sodium channel inhibitor or tolperisone in normalizing or maintaining muscle tone (spasticity).

The teaching of Rundfeldt differs from the claimed invention in the combination use of retigabine and sodium channel blocker such as lidocaine, propagenone and riluzole. To incorporate such teaching into the teaching of Rundfeldt, would have been obvious in view of Cai who teaches the use of sodium channel blocker such as riluzol, lidocaine and propagenone for the treatment of neuropathic pain.

Above references in combination make clear that retigabine and sodium channel blocker such as lidocaine, propageneone and riluzole have been individually used for the treatment of neuropathic pain. It is obvious to combine two compositions each of which is taught by prior art to be useful for same purpose; idea of combining them flows logically from their having been individually taught in the prior art. The combination of active ingredient with the same character is merely the additive effect of each individual component. See In re Kerkhoven, 205 USPQ 1069 (CCPA 1980).

With respect to the determination of various dosage forms (e.g., orally, rectally, intravenously, transdermally, subcutaneously or intracutaneously) and the current administration regimen of two drugs (e.g., simultaneously, separately or consecutively), such determination of appropriate dosage forms and administration regiment for treatment involving each of the above mentioned formulations is routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of drug delivery information provided in the prior art references.

With respect to "said neuralgia pain or neuropathic pain is accompanied by an increase in muscle tone" in claims 26 and 27, the prior art reference(s) does/do not specifically mention the feature of the presence of "an increase in muscle tone" in the prior method. However, one having ordinary skill in the art would have expected at the time of the invention was made that such feature of the instant invention would have been characteristic of the modified prior art method. Especially, considering the state of art knowledge at the time of the invention was made as evidenced by the applicant's admission, one having ordinary skill in the would have expected that the administration of the instant combination containing sodium channel inhibitor would benefit the patient suffering from neuropathic pain accompanying with the increase in muscle tone (spasticity). Thus, one would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

With respect to "human" application of the instant combination, a person having ordinary skill in the art has basis for perceiving those in vivo studies in the cited references as constituting recognized screening procedures with clear relevance to utility in humans.

5. Claims 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rundfeldt et al. (US 6117900) in view of Cai et al. (US 6281211), and further in view of the applicant's admitted prior art of record (page 3, lines 11-23).

The modified teaching of Rundfeldt (Rundfeldt in combination with Cai) includes all that is recited in the claims 14 and 15 except the use of"tolperisone, eprisone and silperisone". The admitted prior art of record teaches tolperisone as sodium channel blocker similar to lidocaine.

One having ordinary skill in the art would have expected that tolperisone would behave similar as to the known sodium channel blocker such as lidocaine and provide therapeutic utility in the treatment of neuropathic pain through sodium channel blocking mechanism. One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01 (a).

Response to Arguments

6. Applicant's arguments filed 02/19/2009 have been fully considered but they are not persuasive.

The applicant's argument in the response takes the position that the examiner's interpretation of "sodium channel" is not consistent with common usage by those skilled in the

art. The applicant alleges that none of the enumerated symporters, cotransporters and exchangers belongs to the classifications of Ion Pumps or Monosaccharide Transport Proteins.

This argument is not found persuasive. Unlike the applicant's argument, given "broadest reasonable interpretation", the instant "a sodium channel-inhibiting substance" is construed to include not only inhibitors of voltage sensitive but also non-sensitive sodium channels activation and other substances as long as they possess the property of either directly or indirectly inhibiting sodium channel, for example inhibitors or antagonists of sodium/hydrogen exchangers, sodium-glucose transporters, sodium/myoinositol cotransporter, Na+/I- symporter, sodium/potassium/calcium exchanger, Na+/K+/CI- cotransporter and etc... (see for example Zani et al., Am J Physiolo Heart Cir. Physiol 288: H89-H95, 2005). Thus, the examiner maintains the rejection of record.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, again, the prior art references in combination (Rundfelt and Cai) make clear that retigabine and sodium channel blocker such as lidocaine, propageneone and riluzole have been individually used for the treatment of neuropathic pain. It is obvious to combine two compositions each of which is taught by prior art to be useful for same purpose; idea of

combining them flows logically from their having been individually taught in the prior art. The combination of active ingredient with the same character is merely the additive effect of each individual component. See In re Kerkhoven, 205 USPQ 1069 (CCPA 1980). Thus, in absence of superior or unexpected results of the combination (generally by showing data or result that the claimed combination achieves unexpected or superior results), the examiner maintains the rejection of the record.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614